

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

1. (Currently Amended) A glycopeptide of the formula  $A_1-A_2-A_3-A_4-A_5-A_6-A_7$ , SEQ ID NO:1 in which each dash represents a covalent bond; wherein the group  $A_1$  comprises a modified or unmodified  $\alpha$ -amino acid residue, alkyl, aryl, aralkyl, alkanoyl, aroyl, aralkanoyl, heterocyclic, heterocyclic-carbonyl, heterocyclic-alkyl, heterocyclic-alkyl-carbonyl, alkylsulfonyl, arylsulfonyl, guanidinyl, carbamoyl, or xanthyl; where each of the groups  $A_2$  to  $A_7$  comprises a modified or unmodified  $\alpha$ -amino acid residue, whereby (i) the group  $A_1$  is linked to an amino group on the group  $A_2$ , (ii) each of the groups  $A_2$ ,  $A_4$  and  $A_6$  (bears an aromatic side chain, which aromatic side chains are cross-linked together by two or more covalent bonds, and (iii) the group  $A_7$  bears a terminal carboxyl, ester, amide, or N-substituted amide group;

and wherein one or more of the groups  $A_1$  to  $A_7$  is linked via a glycosidic bond to one or more glycosidic groups each having one or more sugar residues; wherein at least one of said sugar residues is a disaccharide modified to bear one or more substituents of the formula  $YXR$ ,  $N^+(R_1)=CR_2R_3$ ,  $N=PR_1R_2R_3$ ,  $N^+R_1R_2R_3$  or  $P^+R_1R_2R_3$  in which the group  $Y$  is a single bond, O,  $NR_1$  or S; the group  $X$  is O,  $NR_1$ , S,  $SO_2$ ,  $C(O)O$ ,  $C(O)S$ ,  $C(S)O$ ,  $C(S)S$ ,  $C(NR_1)O$ ,  $C(O)NR_1$ , or halo (in which case  $Y$  and  $R$  are absent); and  $R$ ,  $R_1$ ,  $R_2$ , and  $R_3$  are independently hydrogen, alkyl, aryl, aralkyl, alkanoyl, aroyl, aralkanoyl, heterocyclic, heterocyclic-carbonyl, heterocyclic-alkyl, heterocyclic-alkyl-carbonyl, alkylsulfonyl or arylsulfonyl; and any pharmaceutically acceptable salts thereof; provided that at least one of the substituents of the formula  $YXR$  is not hydroxyl;  $X$  and  $Y$  are not both O;  $X$  and  $Y$  are not S and O, or O and S, respectively; and if two or more of said substituents are present, they can be the same or different; and

provided that when  $A_4$  is linked to a disaccharide having a glucose residue that bears an N-substituted aminohexose residue, then said glucose residue is modified to bear at least one of said substituents  $YXR$ ,  $N^+(R_1)=CR_2R_3$ ,  $N=PR_1R_2R_3$ ,  $N^+R_1R_2R_3$  or  $P^+R_1R_2R_3$ .

2. (Original) The glycopeptide of claim 1 in which said disaccharide comprises two hexose residues linked to  $A_4$  and wherein at least the hexose residue linked directly to  $A_4$  is modified to bear at least one of said substituents  $YXR$ ,  $N^+(R_1)=CR_2R_3$ ,  $N=PR_1R_2R_3$ ,  $N^+R_1R_2R_3$  or  $P^+R_1R_2R_3$ .

3. (Original) The glycopeptide of claim 2 in which said substituent is attached to the C6 position of said hexose residue linked directly to  $A_4$ .

4. (Original) The glycopeptide of claim 3 in which said hexose residue linked directly to  $A_4$  is glucose.

5. (Original) The glycopeptide of claim 4 in which at least one of said substituents is  $YXR$  wherein Y is a single bond and X is O,  $NR_1$ , S or  $SO_2$ .

6. (Original) The glycopeptide of claim 5 wherein X is  $NR_1$ .

7. (Original) The glycopeptide of claim 5 wherein X is S.

8. (Original) The glycopeptide of claim 5 wherein X is  $SO_2$ .

9. (Original) The glycopeptide of claim 5 wherein X is O and R is not H.
10. (Original) The glycopeptide of claim 4 wherein at least one of said substituents YXR is halogen.
11. (Currently Amended) The glycopeptide of claim 2 wherein A<sub>1</sub>-A<sub>2</sub>-A<sub>3</sub>-A<sub>4</sub>-A<sub>5</sub>-A<sub>6</sub>-A<sub>7</sub>, SEQ ID NO:1, form a dalbaheptide.
12. (Currently Amended). The glycopeptide of claim 3 wherein A<sub>1</sub>-A<sub>2</sub>-A<sub>3</sub>-A<sub>4</sub>-A<sub>5</sub>-A<sub>6</sub>-A<sub>7</sub>, SEQ ID NO:1, form a dalbaheptide.
13. (Currently Amended). The glycopeptide of claim 4 wherein A<sub>1</sub>-A<sub>2</sub>-A<sub>3</sub>-A<sub>4</sub>-A<sub>5</sub>-A<sub>6</sub>-A<sub>7</sub>, SEQ ID NO:1, form a dalbaheptide.
14. (Currently Amended). The glycopeptide of claim 5 wherein A<sub>1</sub>-A<sub>2</sub>-A<sub>3</sub>-A<sub>4</sub>-A<sub>5</sub>-A<sub>6</sub>-A<sub>7</sub>, SEQ ID NO:1, form a dalbaheptide.
15. (Currently Amended). The glycopeptide of claim 6 wherein A<sub>1</sub>-A<sub>2</sub>-A<sub>3</sub>-A<sub>4</sub>-A<sub>5</sub>-A<sub>6</sub>-A<sub>7</sub>, SEQ ID NO:1, form a dalbaheptide.
16. (Currently Amended). The glycopeptide of claim 7 wherein A<sub>1</sub>-A<sub>2</sub>-A<sub>3</sub>-A<sub>4</sub>-A<sub>5</sub>-A<sub>6</sub>-A<sub>7</sub>, SEQ ID NO:1, form a dalbaheptide.

17. (Currently Amended). The glycopeptide of claim 8 wherein A<sub>1</sub>-A<sub>2</sub>-A<sub>3</sub>-A<sub>4</sub>-A<sub>5</sub>-A<sub>6</sub>-A<sub>7</sub>, SEQ ID NO:1, form a dalbaheptide.
18. (Currently Amended). The glycopeptide of claim 9 wherein A<sub>1</sub>-A<sub>2</sub>-A<sub>3</sub>-A<sub>4</sub>-A<sub>5</sub>-A<sub>6</sub>-A<sub>7</sub>, SEQ ID NO:1, form a dalbaheptide.
19. (Currently Amended). The glycopeptide of claim 10 wherein A<sub>1</sub>-A<sub>2</sub>-A<sub>3</sub>-A<sub>4</sub>-A<sub>5</sub>-A<sub>6</sub>-A<sub>7</sub>, SEQ ID NO:1, form a dalbaheptide.
20. (Original) The glycopeptide of claim 11, wherein A<sub>6</sub> in said dalbaheptide is linked via a glycosidic bond to one or more sugar residues.
21. (Original) The glycopeptide of claim 11 wherein the amino acids in said dalbaheptide are those in vancomycin.
22. (Original) The glycopeptide of claim 20 wherein A<sub>1</sub>, which is N-methyl leucine, has been selectively removed and replaced with another of said groups A<sub>1</sub>.
23. (Original) The glycopeptide of claim 2 in which the other hexose residue bears at least one of said substituents.
24. (Original) The glycopeptide of claim 3 in which the other hexose residue bears at least one of said substituents.

25. (Original) The glycopeptide of claim 4 in which the other hexose residue bears at least one of said substituents.

26. (Original) The glycopeptide of claim 5 in which the other hexose residue bears at least one of said substituents.

27. (Original) The glycopeptide of claim 6 in which the other hexose residue bears at least one of said substituents.

28. (Original) The glycopeptide of claim 7 in which the other hexose residue bears at least one of said substituents.

29. (Original) The glycopeptide of claim 8 in which the other hexose residue bears at least one of said substituents.

30. (Original) The glycopeptide of claim 9 in which the other hexose residue bears at least one of said substituents.

31. (Original) The glycopeptide of claim 10 in which the other hexose residue bears at least one of said substituents.

32. (Original) The glycopeptide of claim 11 in which the other hexose residue bears at least one of said substituents.

33. (Original) The glycopeptide of claim 12 in which the other hexose residue bears at least one of said substituents.

34. (Original) The glycopeptide of claims 13 in which the other hexose residue bears at least one of said substituents.

35. (Original) The glycopeptide of claims 14 in which the other hexose residue bears at least one of said substituents.

36. (Original) The glycopeptide of claim 23 wherein at least one of said substituents is YXR wherein Y is a single bond and X is O, NR<sub>1</sub>, S or SO<sub>2</sub>.

37. (Original) The glycopeptide of claim 36 wherein X is NR<sub>1</sub>.

38. (Original) The glycopeptide of claim 37 wherein said substituent is attached to C3 of said other hexose residue.

39. (Original) A chemical library comprising a plurality of glycopeptides, each of said glycopeptides having the formula A<sub>1</sub>-A<sub>2</sub>-A<sub>3</sub>-A<sub>4</sub>-A<sub>5</sub>-A<sub>6</sub>-A<sub>7</sub>, in which each dash represents a covalent bond; wherein the group A<sub>1</sub> comprises a modified or unmodified  $\alpha$ -amino acid residue, alkyl, aryl, aralkyl, alkanoyl, aroyl, aralkanoyl, heterocyclic, heterocyclic-carbonyl, heterocyclic-alkyl, heterocyclic-alkyl-carbonyl, alkylsulfonyl, arylsulfonyl, guanidinyl, carbamoyl, or xanthyl; where each of the groups A<sub>2</sub> to A<sub>7</sub> comprises a modified or unmodified  $\alpha$ -amino acid residue, whereby (i) the group A<sub>1</sub> is linked to an amino group on

the group A<sub>2</sub>, (ii) each of the groups A<sub>2</sub>, A<sub>4</sub> and A<sub>6</sub> bears an aromatic side chain, which aromatic side chains are cross-linked together by two or more covalent bonds, and (iii) the group A<sub>7</sub> bears a terminal carboxyl, ester, amide, or N-substituted amide group;

and wherein one or more of the groups A<sub>1</sub> to A<sub>7</sub> is linked via a glycosidic bond to one or more glycosidic groups each having one or more sugar residues; wherein at least one of said sugar residues is a disaccharide modified to bear one or more substituents of the formula YXR, N<sup>+</sup>(R<sub>1</sub>)=CR<sub>2</sub>R<sub>3</sub>, N=PR<sub>1</sub>R<sub>2</sub>R<sub>3</sub>, N<sup>+</sup>R<sub>1</sub>R<sub>2</sub>R<sub>3</sub> or P<sup>+</sup>R<sub>1</sub>R<sub>2</sub>R<sub>3</sub> in which the group Y is a single bond, O, NR<sub>1</sub> or S; the group X is O, NR<sub>1</sub>, S, SO<sub>2</sub>, C(O)O, C(O)S, C(S)O, C(S)S, C(NR<sub>1</sub>)O, C(O)NR<sub>1</sub>, or halo (in which case Y and R are absent); and R, R<sub>1</sub>, R<sub>2</sub>, and R<sub>3</sub> are independently hydrogen, alkyl, aryl, aralkyl, alkanoyl, aroyl, aralkanoyl, heterocyclic, heterocyclic-carbonyl, heterocyclic-alkyl, heterocyclic-alkyl-carbonyl, alkylsulfonyl or arylsulfonyl; and any pharmaceutically acceptable salts thereof; provided that at least one of the substituents of the formula YXR is not hydroxyl; X and Y are not both O; X and Y are not S and O, or O and S, respectively; and if two or more of said substituents are present, they can be the same or different; and

provided that when A<sub>4</sub> is linked to a disaccharide having a glucose residue that bears an N-substituted aminohexose residue, then said glucose residue is modified to bear at least one of said substituents YXR, N<sup>+</sup>(R<sub>1</sub>)=CR<sub>2</sub>R<sub>3</sub>, N=PR<sub>1</sub>R<sub>2</sub>R<sub>3</sub>, N<sup>+</sup>R<sub>1</sub>R<sub>2</sub>R<sub>3</sub> or P<sup>+</sup>R<sub>1</sub>R<sub>2</sub>R<sub>3</sub>.

40. (Original) The chemical library of claim 39 wherein A<sub>1</sub>-A<sub>2</sub>-A<sub>3</sub>-A<sub>4</sub>-A<sub>5</sub>-A<sub>6</sub>-A<sub>7</sub> form a dalbaheptide and wherein said disaccharide comprises two hexose residues linked to A<sub>4</sub> and wherein at least the hexose residue linked directly to A<sub>4</sub> is modified to bear said substituent at the C6 position.

41. (Original) The chemical library of claim 40 wherein the other hexose residue bears a group YXR in which Y is a single bond and X is NR<sub>1</sub>.

42. (Original) A method for preparing a glycopeptide comprising the steps of:

(a) selecting a protected glycopeptide of the formula A<sub>1</sub>-A<sub>2</sub>-A<sub>3</sub>-A<sub>4</sub>-A<sub>5</sub>-A<sub>6</sub>-A<sub>7</sub>, in which each dash represents a covalent bond; wherein the group A<sub>1</sub> comprises a modified or unmodified α-amino acid residue, alkyl, aryl, aralkyl, alkanoyl, aroyl, aralkanoyl, heterocyclic, heterocyclic-carbonyl, heterocyclic-alkyl, heterocyclic-alkyl-carbonyl, alkylsulfonyl, (arylsulfonyl, guanidiny, carbamoyl, or xanthyl; where each of the groups A<sub>2</sub> to A<sub>7</sub> comprises a modified or unmodified α-amino acid residue, whereby (i) the group A<sub>1</sub> is linked to an amino group on the group A<sub>2</sub>, (ii) each of the groups A<sub>2</sub>, A<sub>4</sub> and A<sub>6</sub> bears an aromatic side chain, which aromatic side chains are cross-linked together by two or more covalent bonds, and (iii) the group A<sub>7</sub> bears a terminal carboxyl, ester, amide, or N-substituted amide group;

at least A<sub>4</sub> is linked to a glycosidic group which has a hexose residue linked to A<sub>4</sub>; and said protected glycopeptide has no free amino or carboxyl groups and has a free primary hydroxyl group only at the 6-position of said hexose residue;

(b) contacting said protected glycopeptide with a compound ArSO<sub>2</sub>G in which Ar is an aryl group and G is a leaving group under conditions effective to allow reaction of said free primary hydroxyl group to form a glycopeptide sulfonate ester;

(c) contacting said glycopeptide sulfonate ester with a nucleophile under conditions effective to allow displacement of a sulfonate group to produce a substituted glycopeptide.



43. (Original) The method of claim 42 in which said nucleophile is a thiol compound.
44. (Original) The method of claim 42 in which said nucleophile is a halide.
45. (Original) The method of claim 44 in which said halide-substituted glycopeptide is contacted with a second nucleophile under conditions effective to allow displacement of said halide to produce a second substituted glycopeptide.
46. (Original) The method of claim 45 in which said second nucleophile is a thiol compound.
47. (Original) The method of claim 42 in which the nucleophile is an azide ion, and further comprising reduction of an azido group at the 6-position of the substituted glycopeptide to an amino group.
48. (Original) The method of claim 47 further comprising the step of introducing a substituent onto said amino group.
49. (Original) The method of claim 42 in which the nucleophile is an azide ion, and further comprising a step of contacting said substituted glycopeptide with a phosphine compound under conditions effective to allow formation of an iminophosphorane.

50. (Original) A method for producing the chemical library of claim 39, said method comprising at least two steps in each of which a substituent is introduced on a glycopeptide.

51. (Original) The method of claim 50 wherein at least one of said two steps comprises introducing a substituent on the 6-position of a hexose residue directly linked to A<sub>4</sub>.

52. (Original) The method of claim 51 wherein the other of said at least two steps comprises introducing an N-substituent on an aminohexose residue bonded to said hexose residue directly linked to A<sub>4</sub>.

53. (Original) The method of claim 52 wherein said hexose residue directly linked to A<sub>4</sub> is a glucose residue.

54. (Original) The method of claim 51 wherein A<sub>1</sub>-A<sub>2</sub>-A<sub>3</sub>-A<sub>4</sub>-A<sub>5</sub>-A<sub>6</sub>-A<sub>7</sub> form a dalbaheptide.

55. (Original) The method of claim 54 wherein the amino acids in said dalbaheptide are those in vancomycin.

56. (Original) The method of claim 55 wherein A<sub>1</sub> which is N-methyl leucine, has been selectively removed and replaced with another of said groups A<sub>1</sub>.

57. (Original) A method of preparing a glycopeptide comprising:

- (a) selecting: (i) an aglycone that is soluble in one or more organic solvents, is derived from a glycopeptide antibiotic, and which aglycone has exactly one free phenolic hydroxyl group; and (ii) a protected first glycosyl donor;
- (b) allowing a first non-enzymatic glycosylation reaction to proceed in an organic solvent such that a first glycosidic bond is formed, which links said free phenolic hydroxyl group to the anomeric carbon of the first glycosyl donor to provide a pseudoaglycone having a protected first glycosyl residue;
- (c) selectively removing one protecting group from the first glycosyl residue to provide a pseudoaglycone bearing exactly one free hydroxyl group on the first glycosyl residue;
- (d) selecting a second protected glycosyl donor; and
- (e) allowing a second non-enzymatic glycosylation reaction to proceed in an organic solvent such that a second glycosidic bond is formed, which links said free hydroxyl group on the pseudoaglycone to the anomeric carbon of the second glycosyl donor.

58. (Original) A method of preparing a glycopeptide comprising:

- (a) selecting a protected glycopeptide antibiotic that is soluble in one or more organic solvents,
- (b) contacting the glycopeptide antibiotic with a Lewis acid, and allowing a degradation reaction to proceed such that a sugar residue is removed, producing a pseudoaglycone having exactly one free hydroxyl group on a sugar residue of the pseudoaglycone;
- (c) selecting a protected glycosyl donor; and

(d) allowing a non-enzymatic glycosylation reaction to proceed in an organic solvent such that a glycosidic bond is formed which links the free hydroxyl group on the pseudoaglycone to the anomeric carbon of the glycosyl donor.

59. (Original) The method of claim 57 in which each of the first glycoside and the second glycosyl donor is a monosaccharide bearing an activated anomeric sulfoxide group.

60. (Original) The method of claim 58 in which the glycosyl donor is a monosaccharide bearing an activated anomeric sulfoxide group.

61. (Original) The method of claim 59 in which BF<sub>3</sub> is present in the first non-enzymatic glycosylation reaction.

62. (Original) The method of claim 61 in which the first glycosyl donor is a glucose.

63. (Original) The method of claim 60 in which the glycopeptide antibiotic is vancomycin.

64. (Original) The method of claim 60 in which the glycopeptide antibiotic is vancomycin.

65. (Original) The method of claim 63 in which the Lewis acid is boron trifluoride.

66. (Original) The method of claim 63 in which the glycopeptide antibiotic is rendered soluble in organic solvents by substitution with protecting groups.

67. (Original) The method of claim 66, further comprising removal of said protecting groups subsequent to step (d).

68. (Original) The method of claim 67 in which said protecting groups comprise: aloe groups substituted on amine nitrogens, an allyl ester group, allyl phenolic ether groups, and acetates of aliphatic hydroxyls.

69. (Original) The method of claim 57 in which the aglycone is rendered soluble in organic solvents by substitution with protecting groups.

70. (Original) The method of claim 69, further comprising removal of said protecting groups and protecting groups on the glycosides following step (e).

71. (Original) The method of claim 70 in which said protecting groups comprise: a CBz group on the amine nitrogen, a benzyl ester group, methyl phenolic ether groups on residues 5 and 7, and acetates of aliphatic hydroxyls.

72. (Original) The method of claim 57 in which the glycopeptide is attached to a polymeric support.

73. (Original) The method of claim 58 in which the glycopeptide is attached to a polymeric support.

74. (Original) A method for producing the chemical library of claim 39; said method comprising at least two steps, wherein at least one of said at least two steps comprises a glycosylation reaction which introduces a substituted sugar residue.

75. (Original) The method of claim 74 in which A<sub>1</sub> to A<sub>7</sub> are linked sequentially by peptide bonds and cross-linked as in a dalbaheptide.

76. (Original) The method of claim 75 in which said glycosylation reaction links said substituted sugar residue to an A<sub>4</sub> residue of an aglycone.

77. (Original) The method of claim 76 in which said glycosylation reaction links said substituted sugar residue to a sugar residue of a pseudoaglycone, wherein said sugar residue of a pseudoaglycone is linked to an A<sub>4</sub> residue of the pseudoaglycone.

78. (Original) The method of claim 76 in which a second glycosylation reaction links a second substituted sugar residue to said substituted sugar residue.

79. (Original) The method of claim 77 in which AI is a modified or unmodified  $\alpha$ -amino acid residue, and in which A<sub>1</sub> to A<sub>7</sub> are linked sequentially by peptide bonds and cross-linked so as to have the structure of a dalbaheptide.

80. (Original) The method of claim 78 in which A<sub>1</sub> is a modified or unmodified  $\alpha$ -amino acid residue, and in which A<sub>1</sub> to A<sub>7</sub> are linked sequentially by peptide bonds and cross-linked so as to have the structure of a dalbaheptide.

81. (Original) The method of claim 77 in which the structures and interconnections of A<sub>1</sub> to A<sub>7</sub> are those found in vancomycin.

82. (Original) The method of claim 81 in which a glycosyl donor bearing an activated anomeric sulfoxide group is employed in each glycosylation reaction.

Claims 83-101 (Cancelled)

102. (Original) A glycopeptide antibiotic bearing at least one disaccharide group, said disaccharide group comprising two saccharide groups, a first of said saccharide groups bearing at least one amino or substituted amino group, and a second of said saccharide groups modified to bear at least one substituent which is not hydroxyl, or a pharmaceutically acceptable salt thereof.

103. (Original) The glycopeptide antibiotic of claim 102 wherein the second of said saccharide groups is glucose modified to bear at least one substituent which is not hydroxyl at the C6 position of said glucose.

104. (Original) The glycopeptide antibiotic of claim 103 which is vancomycin modified to bear at least one substituent which is not hydroxyl at the C6 position of said glucose.

105. (Original) The glycopeptide antibiotic of claim 104 wherein said at least one substituent which is not hydroxyl at the C6 position of said glucose is amino.

106. (Original) The glycopeptide antibiotic of claim 105 wherein the first of said saccharide groups bears at least one substituted amino group.

107. (Original) The glycopeptide antibiotic of claim 106 wherein said substituted amino group is  $\text{NR}_1\text{H}$  wherein  $\text{R}_1$  bears one or more alkyl, substituted alkyl, aryl, substituted aryl, heterocyclic or substituted heterocyclic groups.

108. (Original) The glycopeptide antibiotic of claim 107 wherein at least one of said substituted alkyl groups is aralkyl.

109. (Original) The glycopeptide antibiotic of claim 107 wherein at least one of said substituted aryl groups is aralkyloxy substituted aryl.

110. (Original) The glycopeptide antibiotic of claim 107 wherein at least one of said substituted aryl groups is halo substituted aryl.



111. (Original) The glycopeptide antibiotic of claim 102 wherein the first of said saccharide groups bears at least one substituted amino group.

112. (Original) The glycopeptide antibiotic of claim 111 wherein said substituted amino group is  $\text{NR}_1\text{H}$  wherein  $\text{R}_1$  bears one or more alkyl, substituted alkyl, aryl, substituted aryl, heterocyclic or substituted heterocyclic groups.

113. (Original) The glycopeptide antibiotic of claim 112 wherein at least one of said substituted alkyl groups is aralkyl.

114. (Original) The glycopeptide antibiotic of claim 112 wherein at least one of said substituted aryl groups is aralkyloxy substituted aryl.

115. (Original) The glycopeptide antibiotic of claim 112 wherein at least one of said substituted aryl groups is halo substituted aryl.

116. (Original) The glycopeptide antibiotic of claim 112 wherein said at least one substituent which is not hydroxyl is amino.